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Economic evaluation of Zika Contraception Access Network in Puerto Rico during the 2016–17 Zika virus outbreak

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Abstract

Objective: During the 2016-2017 Zika virus (ZIKV) outbreak, the prevention of unintended pregnancies was identified as a primary strategy to prevent birth defects. This study estimated the cost-effectiveness of the Zika Contraception Access Network (Z-CAN), an emergency response intervention that provided women in Puerto Rico with access to the full range of reversible contraception at no cost and compared results with a preimplementation hypothetical cost-effectiveness analysis (CEA).

Study Design: We evaluated costs and outcomes of Z-CAN from a health sector perspective compared to no intervention using a decision tree model. Number of people served, contraception methods mix, and costs under Z-CAN were from actual program data and other input parameters were from the literature. Health outcome measures included the number of Zika-associated microcephaly (ZAM) cases and unintended pregnancies. The economic benefits of the Z-CAN intervention were ZIKV-associated direct costs avoided, including lifetime medical and supportive costs associated with ZAM cases, costs of monitoring ZIKV-exposed pregnancies and infants born from Zika-virus infected mothers, and the costs of unintended pregnancies prevented during the outbreak as a result of increased contraception use through the Z-CAN intervention.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.contraception.2021.10.009.

Results: The Z-CAN intervention cost a total of \$26.1 million, including costs for the full range of reversible contraceptive methods, contraception related services, and programmatic activities. The program is estimated to have prevented 85% of cases of estimated ZAM cases and unintended pregnancies in the absence of Z-CAN. The intervention cost was projected to have been more than offset by \$79.9 million in ZIKV—associated costs avoided, 96% of which were lifetime ZAM-associated costs, as well as \$137.0 million from avoided unintended pregnancies, with total net savings in one year of \$216.9 million. The results were consistent with the previous CEA study.

Conclusion: Z-CAN was likely cost-saving in the context of a public health emergency response setting.

Keywords

Contraception; Cost-effectiveness; Outbreak; Unintended pregnancy; Zika virus

1. Introduction

Zika virus (ZIKV) is a cause of serious birth defects, including brain and eye abnormalities, in approximately 5% of pregnancies with laboratory evidence of possible ZIKV infection [1,2]. During the 2015-2017 ZIKV outbreak, 86% of all cases of laboratory-confirmed ZIKV disease in the United States were reported from Puerto Rico [3,4]. The Centers for Disease Control and Prevention (CDC) identified strategies to prevent pregnancies affected by ZIKV, including the use of contraception as a medical countermeasure to prevent unintended pregnancy among women in Puerto Rico who chose to delay or avoid pregnancy during the ZIKV outbreak [5,6].

Barriers to contraception access across Puerto Rico include inadequate availability of the full-range of reversible contraceptive methods, insufficient provider reimbursement, limited same-day provision, lack of patient education, and shortage of providers trained in insertion, removal, and management of long-acting reversible contraception (LARC) (i.e., intrauterine device [IUD] and implant) [7,8].

With technical assistance from CDC, the National Foundation for the Centers for Disease Control and Prevention (CDC Foundation), an independent nonprofit created by Congress to support CDC's critical health protection work, established the Zika Contraception Access Network (Z-CAN) in 2016. Z-CAN was a short-term emergency response intervention for rapid provision of reversible contraceptive services in Puerto Rico [5,9,10]. Prior to Z-CAN implementation, CDC staff conducted a cost-effectiveness analysis (CEA) relying on published data that suggested increasing contraceptive access at no cost for women in Puerto Rico during a ZIKV outbreak could substantially reduce ZIKV-associated birth defects and overall health care costs [11]. That study calculated that the intervention could reduce lifetime ZIKV-related costs by \$65.2 million and reduce unwanted pregnancy-related medical costs by \$40.4 million [11]. Those results, coupled with growing numbers of cases of ZIKV infection in Puerto Rico, contributed to the deployment of the Z-CAN intervention. Between May 2016 and September 2017, 29,211 women in Puerto Rico received Z-CAN services [9].

This study reports cost-effectiveness estimates of the Z-CAN intervention using updated actual Z-CAN program cost and contraception use data, and compare the results with the estimates from the previously published CEA based on hypothetical costs and outcomes of the planned intervention [11].

2. Material and methods

2.1. The Zika Contraception Access Network intervention

Through Z-CAN, public—private partnerships provided a broad range of opportunities for partners to come together to coordinate efforts among federal and territorial agencies to align strategies, leverage resources, and address sustainability; mobilize private partnerships to secure resources for contraceptive methods and associated services and programmatic activities; and engage key stakeholders to understand context and need, and to identify strategies to reach the target population [12]. The Z-CAN intervention included: (1) provision of the full-range of US Food and Drug Administration (FDA)-approved reversible contraceptive methods at no-cost to the woman; (2) training on client-centered contraceptive counseling and LARC insertion and removal procedures; (3) proctoring and post-training mentorship on delivery of high quality contraceptive services; (4) access to no-cost LARC removal for women who received a LARC method through the Z-CAN intervention after the intervention ended; and (5) health communication campaign. All women of reproductive age without history of permanent contraception were eligible to receive Z-CAN services, irrespective of income or insurance status [5,6,10].

2.2. Analytic methods

We adapted the decision tree previously developed at CDC to estimate the cost-effectiveness of the Z-CAN intervention in comparison to the “status quo” without the Z-CAN intervention (Fig. 1) [11]. The decision tree branches at the node represent different decision scenarios and the consequences of each scenario [13]. The CEA multiplied the expected probabilities of each event occurring, e.g., a pregnancy affected by ZIKV, by the expected costs and health outcomes associated with that node in the decision tree, and summed across all nodes for each branch of the decision tree. Intervention costs were based on Z-CAN program data; costs of outcomes were from the literature. The expected values of costs and outcomes for each scenario were used to calculate the relative cost-effectiveness of the scenarios. A scenario with lower costs and better outcomes than other scenarios is classified as a “dominant” or “cost-saving” intervention; otherwise, incremental cost-effectiveness ratios are calculated.

All analyses were conducted using TreeAge Pro 2018 software (TreeAge Software, Williamstown, MA). All costs were adjusted to 2019 U.S. medical prices using the health component of the Personal Consumption Expenditure Price Index [14].

The main or “base-case” CEA used point estimates of the most likely values for each model input to estimate costs and outcomes [15]. We also conducted one-way sensitivity analyses using ranges of estimates for uncertain model inputs to assess the potential impact of the key parameters on the cost-effectiveness estimates of Z-CAN (supplementary materials). In

addition, a probabilistic sensitivity analysis was conducted using Monte Carlo simulation (10,000 draws) in combinations with specified probability distributions for all parameters in the model to estimate the probability that the program would be regarded as cost saving [16].

Health outcome measures included numbers of cases of ZIKV-associated microcephaly (ZAM), defined as second trimester pregnancies with ZAM resulting in live-born infants, miscarriages and stillbirths, or elective terminations of a fetus with microcephaly. We did not include other ZIKV-associated birth defects [17], given we did not have epidemiological or cost estimates for these conditions. We also estimated the number of unintended pregnancies avoided and the avoided medical costs from prevention of unintended pregnancies. An unintended pregnancy in general is a pregnancy that occurred either when no children or no more children were desired or the pregnancy occurred earlier than desired [18]. Given that Z-CAN participants were actively pursuing contraception to avoid or delay pregnancy, we assumed that all pregnancies of Z-CAN participants were unintended during the current year.

Economic benefits of the Z-CAN intervention included lifelong cost avoided from ZAM cases prevented, cost avoided due to enhanced monitoring of ZIKV-exposed pregnancies and infants born from ZIKV infected mothers, and cost avoided from unintended pregnancies (i.e., prenatal, delivery, postpartum, and infant care up to 3 months after birth) as a result of increased contraception access and utilization through Z-CAN. Lifetime costs were calculated as a present value of costs in future years, at 2019 prices, discounted back to the present using a 3% discount rate. We calculated net savings as the total cost avoided relative to the status quo minus the intervention cost.

A study time frame of 17 months was used, corresponding to the time frame of Z-CAN implementation (May 2016–August 2017). The analytical time horizon for pregnancy outcomes, spanned from the start of Z-CAN implementation to 9 months after the last group of women received the Z-CAN intervention and a life-time analytical horizon for long-term infant outcomes associated with ZAM.

The text in the supplementary materials describes the details of the model input parameters [1,9,17,19–27,33,34]. The contraception use and method mix before and after the Z-CAN intervention (Supplementary Table 1), and the costs of Z-CAN program activities (Supplementary Table 2) were the key input parameters in the decision tree model to calculate the effectiveness and cost of Z-CAN. The other epidemiological and cost parameters used in the model are described in Supplementary Table 1.

3. Results

3.1. Base-case analysis

The overall total cost for the Z-CAN intervention was \$26.1 million (Supplementary Table 2). The total programmatic cost was \$4.9 million dollars (\$168 per participant), including \$491,036 for training, \$78,836 for proctoring, \$2.8 million for administrative costs, and \$1.5 million for the health communication campaign (Supplementary Table 2). The total costs for providing the full range of reversible contraceptive methods was \$17.4 million,

including \$14.1 million for highly effective contraception (IUD and implant), \$3.3 million for moderately effective contraception (injection, pill, patch, and ring), and \$30,239 for less effective contraception (condom) (Supplementary Table 2). The incremental cost of the Z-CAN intervention, i.e., implementing Z-CAN and providing contraception as compared to contraception services under the status quo was \$21.7 million (Table 1).

The Z-CAN intervention was predicted to prevent 26 cases (85% of the cases under the no-intervention scenario) of ZIKV-associated microcephaly, among which 24 would have resulted in live birth. Comparing Z-CAN with the status quo, the total lifetime ZIKV-associated discounted cost was estimated at \$101.7 million (in 2019 US dollars), including \$97.1 million from lifetime ZIKV-associated microcephaly cost avoided, and \$4.5 million for cost avoided from testing and monitoring for ZIKV during pregnancy and after delivery for infants (Table 1). The net savings subtracting the costs incurred under the Z-CAN intervention from the cost incurred under the status quo, only taking into account health outcomes and costs associated with testing and monitoring for ZIKV infection and ZIKV-associated microcephaly, was \$79.9 million. When considering the additional \$137.0 million net cost avoided from avoiding 9649 unintended pregnancies prevented with Z-CAN, total net savings of Z-CAN was \$216.9 million.

3.2. Sensitivity analyses

Z-CAN was calculated to be cost saving in all sensitivity analyses. The lowest estimate, \$63.6 million, is from an analysis in which base-case health care costs were adjusted to Puerto Rico prices (supplementary materials 1). The highest estimate of cost savings, \$264.5 million, assumed the base-case cost inputs with a higher (7/1000) prevalence of ZIKV-associated microcephaly (Table 2). The probabilistic sensitivity analysis scatter graph shows that in all of the simulation scenarios the intervention scenario had lower costs and more cases of ZIKV-associated microcephaly prevented compared with the no intervention scenario (Supplementary Figure 1). Sensitivity analyses showed that the estimated savings from unintended pregnancies did not change in most of the scenarios, except when medical costs in Puerto Rico were assumed; in that scenario the net savings from unintended pregnancies prevented was only \$48.7 million (Table 2). When only considering only unwanted pregnancies, the cost savings from avoided pregnancies was \$54.8 million, for a total net savings of \$136.7 million.

4. Discussion

Using actual program cost and updated epidemiological data, this analysis demonstrates that the Z-CAN intervention could be cost saving in the context of a public health emergency response setting. The program is estimated to have prevented 85% of cases of estimated ZAM cases and unintended pregnancies in the absence Z-CAN. The intervention cost was projected to have been more than offset by \$101.7 million in ZIKV—associated costs avoided, as well as \$137.0 million from avoided unintended pregnancies, with total net savings in one year of \$216.9 million. The conclusion that Z-CAN could be cost saving was consistent with the previous CEA of a hypothetical Z-CAN like intervention before Z-CAN

was implemented. The absolute amount of the savings was larger than in the previous CEA: \$88.4 million savings vs \$31.7 million from preventing lifetime ZIKV-associated costs.

In the previous CEA, data from literature were used to simulate cost-effectiveness of a hypothetical Z-CAN-like program, and assumptions were made regarding key parameters, including baseline contraception use, anticipated changes in contraception use under the intervention, and the prevalence of ZIKV-associated microcephaly among second-trimester pregnancies [11]. Given the limited information available for the hypothetical intervention in the previous CEA, a conservative approach was deliberately taken for estimating the impact of the intervention to increase access to LARC methods. The actual proportion of women selecting a LARC method was much higher in the Z-CAN intervention compared with the hypothetical intervention (69% vs 19.2%) and was very similar to the CHOICE project [28]. In the previous CEA, sensitivity analyses demonstrated greater cost effectiveness with higher uptake of LARC methods. These factors likely contribute to the larger savings from the real Z-CAN program comparing to the previous CEA using hypothetical data.

The key epidemiological parameters used in the previous CEA and the current CEA using real-world data were similar. In the previous study, the prevalence of ZIKV-associated microcephaly among second trimester pregnancies based on modeling was 5.8/1000. In the current study using ZIKV surveillance data [17], the prevalence was 4.7/1000, suggesting that modeling at the beginning of the ZIKV outbreak was reasonably accurate.

Our study has 2 important contributions. First, cost data for a real-world large-scale public health intervention during an emergency response can inform estimates for similar programs in the future. We provide detailed cost information for different activities in the Z-CAN intervention. Second, we had a unique opportunity to conduct a CEA for a hypothetical intervention prior to implementation, and conduct another economic evaluation using actual costs of the real-world intervention. The findings are consistent and validate modeling as a useful way to plan and justify interventions prospectively using estimates based on literature to inform decision-making in an emergency setting with many uncertainties and retrospectively using program data to evaluate the effectiveness and cost-effectiveness of programs.

There are several limitations to this analysis. We relied on mathematical modeling to estimate the numbers of pregnancies and resulting cases of ZIKV-associated microcephaly based on the contraception distribution with and without the intervention, as is common for cost-effectiveness analyses of contraception [29–31]. We assumed that participants would not have changed birth control methods or started birth control without Z-CAN. Pregnancy losses could be underestimated since pregnancy loss is difficult to capture, ZIKV is often asymptomatic or mild, and laboratory confirmation of ZIKV was required for surveillance. In the sensitivity analysis that used a 50% pregnancy loss rate for secondary trimester pregnancies as an upper bound the intervention was still cost saving.

The estimated cost savings presented are a conservative measure since we did not include other birth defects associated with ZIKV infection such as eye abnormalities and brain abnormalities without microcephaly, due to lack of cost data. We used the prevalence

of brain abnormalities and/or microcephaly as a proxy for ZAM, since there was no ZAM-specific prevalence available and ZAM were often with brain abnormalities. CDC Foundation established a safety net to ensure no-cost LARC removal up to 10 years after the program ended [10], which was not included in the cost analysis, but additional programmatic cost that occurred in future years. Lastly, some parameters were not updated due to lack of new information (e.g., the rate of first trimester pregnancy loss including induced abortion and spontaneous abortion in Puerto Rico, cost of ZIKV-associated birth defects) and the distribution of first trimester pregnancy outcomes, derived from multiple sources. We conducted sensitivity analyses on these parameters. The conclusions remain qualitatively the same.

We only included direct medical costs in the model. We used a health sector perspective that included an estimate of health care payments in Puerto Rico regardless of payer type based on data from US employer-sponsored health plans. A health system perspective was regarded as appropriate from the perspective of a coalition of payers (foundations, pharmaceutical companies, insurers, and government) assembled at the outset of an emergency response to aid in securing financial backing. We did not have information on expenditures by Puerto Rico payers. We were not able to follow a societal perspective because we did not have data on nonmedical costs such as productivity loss of patients with ZAM usually included in a societal perspective or the intangible costs associated with mental distress and anxiety of screening and testing due to Zika infection.

The decrease in cases of ZIKV-associated birth defects in Puerto Rico after February 2017 was aligned with the timing of the Z-CAN intervention—about 9 months after the first group of women participated in Z-CAN [17]. However, it is not clear how much of the reduction in cases was due to the Z-CAN intervention or to other strategies such as vector control programs to reduce disease transmission, a mass media campaign for general ZIKV prevention, and distribution of ZIKV prevention kits [32]. Also, the Z-CAN intervention was not deployed immediately at the onset of the outbreak due to critical steps for program design, partnership building, and capacity building [12]. Implementation of the Z-CAN program at the onset of the public health emergency response might have resulted in delivery of services to an even greater number of women and thus a greater magnitude of effect. However, even if the intervention had been deployed at the onset of the outbreak, there may have been a missed opportunity to prevent unintended pregnancies given barriers to contraceptive access in Puerto Rico before the ZIKV outbreak that Z-CAN addressed. This further illustrates the importance of facilitating access to full contraceptive coverage irrespective of emergency preparedness and response. Previous research reported that prior to the ZIKV outbreak, Puerto Rico had policies that supported contraceptive coverage and services; however, policy implementation specific to access, delivery, and utilization were often limited by administrative, logistical, and financial barriers [35]. The emergency response to the ZIKV outbreak supported an environment for Z-CAN to develop and implement a series of short-term policy and practice changes to improve contraceptive services by aligning efforts and leveraging resources among federal and territorial partners. Although practice change efforts as a result of Z-CAN may be feasible to sustain, including implementation of evidence-based contraceptive guidelines and continuation of additional

contraceptive service access points, consideration of long-term policy and practice changes related to contraceptive access is warranted to address long-term sustainability [35].

This retrospective post-Z-CAN implementation CEA confirmed the cost-effectiveness projections of a preimplementation CEA that was prepared to inform the Z-CAN implementation. That suggests that hypothetical CEAs might be used to inform contraception interventions in future public health emergencies that pose a risk to pregnant women and their infants.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Implications

We demonstrate that Z-CAN, an emergency response intervention for rapid provision of reversible contraception during the 2016-2017 ZIKV outbreak in Puerto Rico, was likely cost saving. Cost-effectiveness modeling can be used to inform decision-making of implementing similar programs for other emergency settings affecting pregnant women and their infants

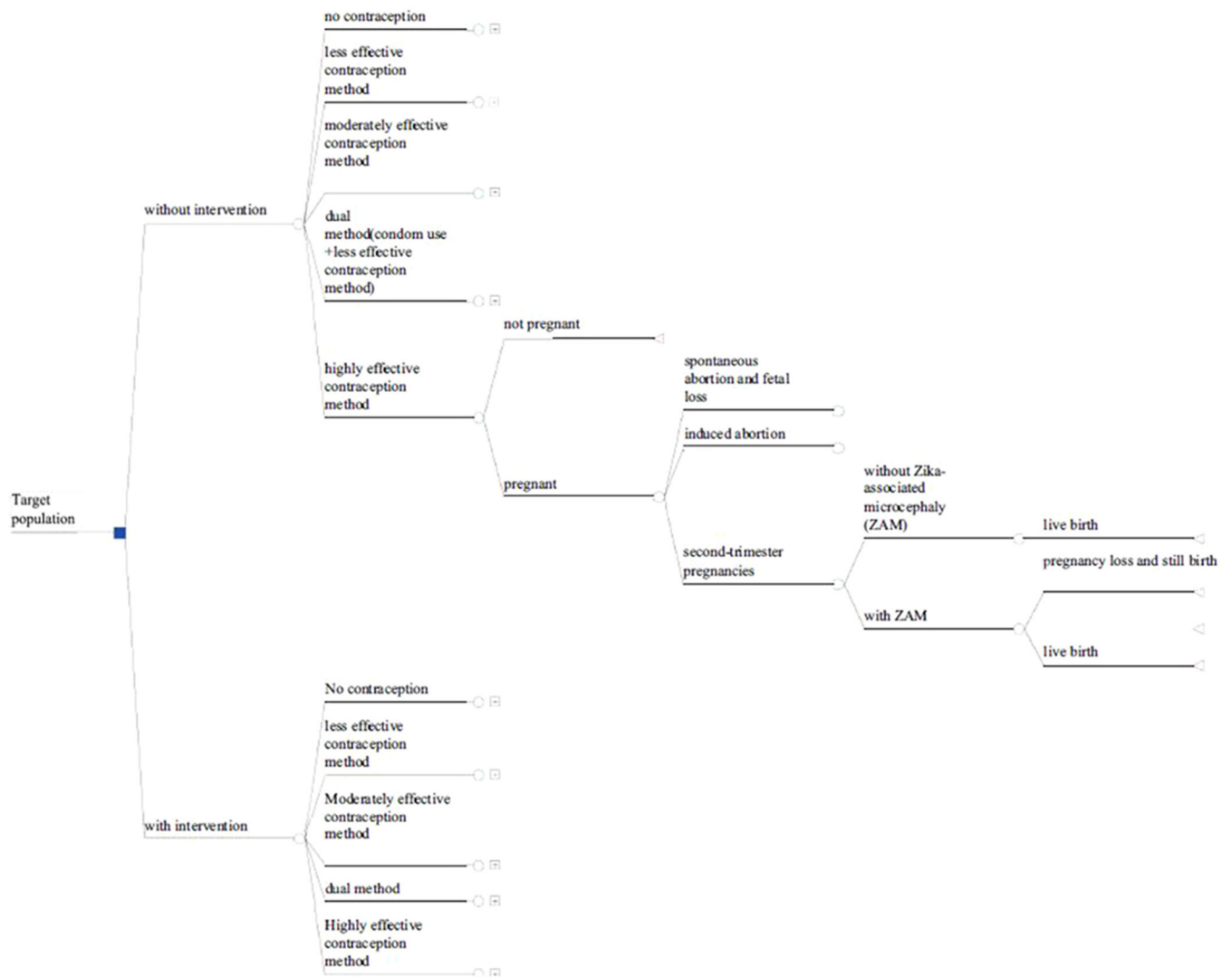


Fig. 1.
Decision tree model structure.

Table 1

Number of Zika virus–associated microcephaly cases and Zika virus–associated costs and number of unintended pregnancies and costs under the scenarios without intervention (status quo) and with the Zika Contraception Access Network (Z-CAN) [†]

Parameter	Without intervention	With intervention	Difference
Prevention of ZAM and Zika virus–associated cost			
Total no. of ZAM cases	31	4.6	–26
No. live births	28	4.2	–24
Total Zika virus–associated cost	\$119,646,575	\$17,996,046	–\$101,650,529
Costs of zika testing and monitoring [§]	\$5,313,065	\$799,282	–\$4,513,783
Direct costs of ZAM [¶]	\$114,333,509	\$17,196,764	–\$97,136,745
Pregnancy loss ^ℳ	\$14,357	\$2,159	–\$12,198
Live births			
Cost savings from Zika virus–associated cost only [#]	\$124,033,916	\$44,090,309	–\$79,943,607
Prevention of unintended pregnancies			
No. of unintended pregnancies ^{**}	11,357	1,708	–9,649
Total medical cost associated with unintended pregnancy	161,200,362	24,250,278	–136,950,084
Net cost savings from avoiding both Zika virus–associated cost and unintended pregnancy cost ^{††}			–\$216,893,691

ZAM, Zika virus–associated microcephaly. All costs are adjusted to U.S. 2019 dollars.

[†]The numbers in the columns and rows might not exactly match because of rounding.

^{*}With intervention scenario also includes Z-CAN program cost.

[§]Costs of extra testing and monitoring for Zika virus during pregnancy and for infants exposed in utero during Zika virus outbreak. Only including cost of testing for Zika virus and monitoring for exposed infants without ZAM; testing costs for infants with ZAM are included in the direct costs of ZAM.

[¶]Costs include direct medical and medical-related costs, including supportive care for persons with ZAM, even if the cost might not be paid by health care payers or delivered by health care providers.

^ℳIncluding still birth and termination of fetus with ZAM. Direct costs of ZAM include both costs of pregnancy loss and live births.

[#]Total Zika virus–associated cost avoided (absolute value) minus the additional cost of family planning service under intervention compared with no intervention.

^{††}Absolute value of net medical cost for unintended pregnancy plus absolute value of net cost savings from Zika virus–associated costs avoided.

Table 2

Sensitivity analyses indicating the number of ZAM cases prevented and Zika virus–associated costs avoided in proposed intervention to increase access to contraception to women during Zika virus outbreak, Puerto Rico, 2016^{*}

Parameter	No. ZAM cases prevented	Incremental intervention cost [†] millions	Zika virus–associated cost avoided, millions	Net savings ^{††} millions	Additional cost avoided from UP, millions	Net savings from both Zika-related costs and UP ^{†,††}
Base-case	26	\$21.7	\$101.7	\$79.9	\$137.0	\$216.9
Rate of ZAM among all live-born infants; main scenario value						
4.7/1000						
3.4/1000	19	\$21.6	\$74.8	\$53.1	\$137.0	\$190.1
7.0/1000	39	\$21.6	\$149.2	\$127.5	\$136.9	\$264.5
Lifetime costs for microcephaly; main scenario value \$3.8 million						
\$0.65 million (break-even scenario) ^{**}	26	\$21.6	\$20.0	–\$1.6	\$137.0	\$135.3
\$3.2 million	26	\$21.6	\$81.8	\$60.1	\$137.0	\$197.1
\$4.9 million	26	\$21.6	\$120.4	\$98.8	\$137.0	\$235.7
Pregnancy loss with ZAM						
50%	26	\$21.6	\$57.4	\$35.7	\$136.7	\$172.4
Annualized LARC device cost	26	\$11.7	\$101.7	\$90.0	\$137.0	\$226.9
Puerto Rico costs ^{***}	26	\$21.6	\$36.5	\$14.9	\$48.7	\$63.6
Discount rate						
0%	26	\$21.6	\$163.9	\$142.2	\$137.0	\$279.2
5%	26	\$21.6	\$81.9	\$60.3	\$137.0	\$197.2
Prevention of unwanted pregnancies only [§]	26	\$21.6	\$81.9	\$60.3	\$54.8	\$136.7

^{*} LARC, long-acting reversible contraceptive; UP, unintended pregnancies; ZAM, Zika virus–associated microcephaly. All costs are adjusted to U.S. 2019 dollars.

[†] Incremental intervention cost is the intervention cost with Z-CAN minus the intervention cost without Z-CAN.

^{††} Net savings is the additional cost of contraception minus Zika virus–associated cost avoided.

^{†††} The number may not be exactly equal to the sum of the numbers in the previous two columns due to rounding.

^{**} The estimated cost of ZAM with which the medical cost avoided from preventing ZAM equals to the incremental intervention costs of Z-CAN scenario, which means the net savings from the intervention is \$0.

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*** To account for differences in health care costs between the continental U.S. and Puerto Rico, the costs for testing and monitoring ZIKV-affected pregnancies and for treatment and supportive care for cases of ZIKV-associated birth defects were adjusted to the prices in Puerto Rico market by applying conversion factors of ratios of health care spending per capita and wages of nurse assistants between the United States and Puerto Rico.

‡ Only from unwanted pregnancies as opposed to mistimed pregnancies which might result in a delayed costs occurring later. Roughly 60% of unintended pregnancies are classified as mistimed and 40% as unwanted.